REMARKS

Status of the Claims

Claims 1-25 were originally pending. Claims 4, 5, 8-13, 21 and 25 have been withdrawn from consideration in response to a restriction requirement and are now cancelled. Claims 1-3, 6, 7, 14-20 and 22-24 are pending. Claims 1-3, 6, 7, 14-20 and 22-24 have been rejected. Reconsideration of the application is respectfully requested.

The Rejections Under 35 U.S.C. §102(b) Should be Withdrawn

Claims 1-3, 6-7, 17, 19-20, and 22-23 remain rejected under 35 U.S.C.102(b) as being anticipated by Bruchez *et al.* (USP No. 6,274,323). The Examiner argues that Bruchez *et al.* teaches a method for assaying a sample for the presence of a target molecule just as required by the claims of the present invention. The Applicant respectfully traverses this rejection.

Bruchez *et al.* does not anticipate the presently claimed invention for two reasons. First, Bruchez *et al.* does not disclose all of the limitations of the claims. Second, Bruchez *et al.* does not enable the present claims.

Bruchez *et al.* does not disclose all of the limitations of Claim 1.

Bruchez *et al.* cannot anticipate Claim1 because it does not disclose all of the limitations of Claim 1. Bruchez *et al.* does not teach a method for assaying a sample for the presence of a target molecule comprising: providing a liquid sample suspected of comprising the target molecule; contacting the sample with a filter, said filter comprising a sensor molecule attached

thereto, said sensor molecule capable of specifically binding to the target molecule, if present; passing the sample transversely through said filter using a pressure-controlling apparatus under conditions that allow the sensor molecule to bind to the target molecule; recovering the remaining liquid sample; and determining whether the target has bound to the sensor.

First, Bruchez *et al.* does not teach or suggest a filter comprising an attached sensor molecule. The Examiner argues that Bruchez *et al.* teaches that semiconductor nanocrystals may be used in competitive microsphere filter assays. In particular, the Examiner argues that in Bruchez *et al.* "...an antibody is conjugated to microspheres that are caught on pore filters." (emphasis added)(page 3 last sentence to the first sentence on page 4). Claim 1 of the present invention teaches a method of:

> providing a liquid sample suspected of comprising the target molecule;
> contacting the sample with a filter, said filter comprising a sensor molecule attached thereto, said sensor molecule capable of specifically binding to the target molecule, if present;
> passing the sample transversely through said filter using a pressure-controlling apparatus under conditions that allow the sensor molecule to bind to the target molecule;
> recovering the remaining liquid sample; and
> determining whether the target has bound to the sensor.

Bruchez *et al.* does not teach or suggest the limitation of claim 1 which recites the limitation of "...a filter comprising a sensor molecule attached thereto." (emphasis added). The terms "caught" and "attached" have very different connotations which become readily more apparent when read in the context of the method taught by Bruchez *et al.*

> "The detection is achieved by competition between analyte in the sample and analyte conjugated to semiconductor nanocrystals or conjugated to a semiconductor nanocrystal-encoded microsphere which is small enough to pass through the filter pores. Separation is achieved because the reaction is free to pass through a microporous filter in which the pores are a smaller size than the diameter of the microsphere. Thus the microsphere cannot pass through the filter (see FIG. 5). Semiconductor nanocrystal-conjugates or semiconductor nanocrystal encoded microspheres are of small enough size to pass through the filter and will do so unless bound to the microspheres. If a known amount of semiconductor nanocrystals are applied to the upper level, with the analyte sample, allowed to bind for a predetermined time and then passed through the filter, the concentration of the analyte is determined by measuring the level of fluorescence present in the lower level. Fluorescence in the upper level is not detected either by removal of the upper level or because the membrane is opaque to the excitation source." (emphasis added)(Column 28, lines 49-67)

Thus, the method taught in Bruchez *et al.* is a competition assay in which the analyte binder is bound to a microsphere, not the filter. This can be clearly seen in Figure 5 of Bruchez *et al.* The microspheres are then "caught" in the pores of the filter because they are too large to pass through. Thus, there is no suggestion or teaching in Bruchez *et al.* of a filter comprising a sensor molecule attached thereto. Because Bruchez *et al.* lacks any such teaching it cannot anticipate any of the present claims, all which include a filter comprising a sensor molecule attached thereto.

Second, Bruchez *et al.* does not teach or suggest a method of passing a liquid sample transversely through a filter using a pressure-controlling apparatus under conditions that allow the sensor molecule to bind to a target molecule within the liquid sample. In the Office Action

of December 29, 2005, the Examiner argued that apparatuses such as capillaries, hollow fibers, needles, pins, and the like are capable of controlling the pressure of a liquid sample by limiting the rate and amount of sample taken in. The Applicant disagreed stating that apparatuses such as capillaries, hollow fibers, needles, pins, and the like described in Bruchez *et al.* (see column 22, lines 52-56) are used in Bruchez *et al.* as examples of solid supports, not separate apparatuses. In the Office Action of June 2, 2006, the Examiner does not address the Applicant's reply, but merely states that apparatuses such as capillaries, hollow fibers, needles, pins, and the like are not examples of filters. The Applicant agrees that apparatuses such as capillaries, hollow fibers, needles, pins, and the like are not examples of filters, however, the Applicant also would point out that apparatuses such as capillaries, hollow fibers, needles, pins, and the like are not used anywhere in Bruchez *et al.* as pressure-controlling apparatuses for the passing of a liquid sample transversely through a filter. The Examiner has not pointed to any teaching in Bruchez *et al.* of a method of passing a liquid sample transversely through a filter using a pressure-controlling apparatus under conditions that allow a sensor molecule to bind to a target molecule within the liquid sample. Because Bruchez *et al.* lacks any such teaching it cannot anticipate any of the present claims, all which include a step of using a pressure-controlled apparatus to pass a sample through a filter.

Accordingly, for the reasons stated above, Claim 1 and all claims depending therefrom are allowable. Withdrawal of the rejection is requested.

Bruchez *et al.* cannot anticipate the claims because it is not enabling

As noted previously, Bruchez *et al.* does not suggest or teach the use of a filter comprising a sensor molecule attached thereto. In the present Office action, the Examiner argues that Bruchez *et al.* describes certain microporous membranes as filters. Even assuming, *arguendo*, that some of the microporous membranes described in Bruchez *et al.* can be described as "filters", there is simply no teaching or suggestion in Bruchez *et al.* of the microporous membranes having a sensor molecule attached. As mentioned previously, Bruchez *et al.* describes the conjugation of antibodies to a microsphere, not a filter. In particular, Bruchez *et al.* describes a method for detecting an analyte by which "...the detection is achieved by competition between analyte in the sample and analyte conjugated to semiconductor nanocrystals or conjugated to a semiconductor nanocrystal-encoded microsphere which is small enough to pass through the filter pores." (emphasis added)(Column 28, lines 49-55). As clearly exemplified in Figure 5 of Bruchez *et al.*, there are no sensor molecules attached to the filter. Thus, Bruchez *et al.* cannot anticipate the claim of the present invention because the methods described in Bruchez *et al.* do not teach or suggest a sensor molecule attached to a filter.

Likewise, Bruchez *et al.* also does not teach or suggest passing a liquid sample transversely through a filter using a pressure-controlling apparatus under conditions that allow the sensor molecule to bind to a target molecule within the liquid sample. In the present Office action, the Examiner states that:

> "A sample is passed through the filter and the immobilized antibodies catch any antigen present. If the sample contains no antigen then the enzyme/antigen will bind to the free site on the antibody on the filter. Bruchez *et al.* teaches multiple simultaneous detections. The detection takes place on the filter or in the filtrate and the assay may be carrier out in high throughput multiwell environment. Thus

almost any target molecule, analyte, chemical or biological, organic or inorganic may be detected in this manner. Separation is achieved because the reaction is free to pass through a microporous filter in which the pores are a smaller size then the diameter of the microsphere. Thus the pressure controlling microsphere cannot pass through the filter." (page 4, lines 1-10).

First, at the risk of being redundant, Bruchez *et al.* does not mention or suggest that antibodies are immobilized on a filter. Antibodies are bound to either a solid substrate (such as a microtiter plate) or a microsphere (such as a bead). The Examiner cannot point to any section of Bruchez *et al.* which describes such a technique. Thus, the statement that antigen can be captured by antibodies attached to a filter is clearly erroneous.

Second, in regards to the use of fluid pressure to control the flow of liquid through a filter, the Examiner seems to be arguing that microspheres are somehow controlling the fluid pressure. The Applicant believes that this argument is not supported by the teachings of Bruchez *et al.* There simply is no suggestion anywhere in Bruchez *et al.* of passing a liquid sample transversely through a filter using a pressure-controlling apparatus under conditions that allow the sensor molecule to bind to a target molecule within the liquid sample. In fact the word "pressure" cannot be found anywhere in the specification of Bruchez *et al.* Even assuming, *arguendo*, that some of the apparatuses such as capillaries, hollow fibers, needles, pins, and the like are capable of controlling the pressure of a liquid sample, there is simply no teaching or suggestion in Bruchez *et al.* to use the apparatuses to pass a liquid sample transversely through a filter or that the apparatuses are capable of performing such a function. Thus, the statement that that microspheres are somehow controlling fluid pressure is clearly erroneous.

For the reasons outline above, it is Applicant's position that Bruchez *et al.* does not enable the present claims. "[I]nvalidity by anticipation requires that the four corners of a single, prior art document describe every limitation of the claimed invention, either expressly or inherently, such that a person of ordinary skill in the art could practice the invention without undue experimentation." Advanced Display Systems, Inc. v. Kent State University, 212 F.3d 1272 (Fed. Cir. 2000) (emphasis added). Bruchez *et al.* does not meet this standard.

Accordingly, for the reasons stated above, Claim 1 and all claims depending therefrom are allowable. Withdrawal of the rejection is requested.

In view of the forgoing, Applicants respectfully request that the Examiner withdraw the pending rejections under 35 U.S.C. §102(b).

The Rejections Under 35 U.S.C. §103(a) Should be Withdrawn

Claim 18 remains rejected under 35 U.S.C. 103(a) as being unpatentable over Bruchez *et al.* (USP No. 6,274,323) in view of Hurley *et al.* (USP No. 5,256,571). The Applicant respectfully traverses this rejection.

The Applicant restates the argument made above and in the response to the Office Action of December 29, 2005 that Bruchez *et al.* either alone or in combination, does not teach or suggest passing a liquid sample transversely through a filter using a pressure-controlling apparatus and does not teach or suggest the immobilization of antibodies on a filter. In the present Office Action, the Examiner does respond to the Applicant's arguments but instead restates that Bruchez *et al.* teaches a filter comprising an antibody sensor. Without the teaching

or suggestion of a pressure-controlling apparatus or a filter with attached sensory molecule, Claim 18 can not rendered obvious by Bruchez *et al.*

For all of the above-discussed reasons, Applicant submits that the rejection of Claim 18 under 35 U.S.C. §103(a) have been overcome. Withdrawal of the rejection is requested.

Conclusion

In light of the arguments presented above, Applicants respectfully submit that the claims are in condition for allowance. Early notice to this effect is solicited. It is not believed that extensions of time or fees for net addition of claims are required, beyond those that may otherwise be provided for in documents accompanying this paper. However, in the event that additional extensions of time are necessary to allow consideration of this paper, such extensions are hereby petitioned under 37 CFR § 1.136(a), and any fee required therefore (including fees for net addition of claims) is hereby authorized to be charged to Deposit Account No. 502855 referencing attorney docket number 11.025011.

Respectfully submitted,

Customer No. 0000 38732

By:

Theodore Allen
Registration No. 41,578
Cytyc Corporation
250 Campus Drive
Marlborough, MA 01752
Tel (508) 263-8490
Fax (508) 263-2959